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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,184	10/03/2003	J.H. David Wu	176/61411 (2-11141-03010)	2775

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,184	WU ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-120* is/are pending in the application.

4a) Of the above claim(s) *31-120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Claims 1-120 are pending.

2. Claims 31-120 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-30 drawn to a method of culturing peripheral lymphoid organ cells comprising culturing said cells on a three-dimensional scaffolding are under consideration in the instant application.

3. Applicant's submission that co-pending application 2003/0109042 has been abandoned, obviated the previous rejection of claims 1-30 under provisionally rejection on the ground of nonstatutory obviousness-type double patenting over claims 1-30 of co-pending application 2003/0109042 .

In view of the arguments filed 6/12/02(Paper No. 13), the following rejections remain:

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 22 and 23 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 22 and 23 being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is method step: it is unclear if cells were isolated and reseeded into the new culture medium or if cells with old culture medium were reseeded. Also it is unclear if reseeded step require three-dimensional matrix. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination invention use FP 7.57 and 7.58)

Applicant's arguments, filed 02/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that claims 22 and 23 do not recite "new or old culture mediums and the culture medium recited in claims 22 and 23 clearly refers back to the culture medium of claim 1.

Contrary to Applicant's assertion, it is the Examiner position that claims 22 and 23 are indefinite and ambiguous. Said claims only generally recited seeding or reseeding the culture cells of claim 1. However, as has been stated above, it is unclear if said cells were reseeded into the new culture medium and further requires culturing on a three-dimensional matrix.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-30 stand rejected under 35 U.S.C. 102(a) as being anticipated by WO 01/036589 (IDS) for the same reasons set forth in the previous Office Action, mailed on 08/01/06.

Applicant's arguments, filed 02/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that: the Examiner appears to rest the rejection on the assumption that the bone marrow – derived hematopoietic stem cells taught by WO'589 are peripheral lymphoid organ cells. Said assumption is incorrect as evidence from the Declaration of DR. Bottaro under 37 C.F.R 1.132.

The examiner strongly disagrees with Applicant's interpretation of the Examiner's rejection . Moreover, the Examiner failed to find any support for said assumption in the previous Office Action rejection mailed on 08/01/06. It is the Examiner position that WO' 589 does not limited the disclosed method for culturing only hematopoietic stem cells. Applicant's attention is respectively drawn to pages 4, 5, 9 and 18 in particular. WO' 589 explicitly teaches that the disclosed three-dimensional culture system is suitable for culturing stromal cells, T and B lymphocytes, APC, NK cells memory cells etc. As is evidenced form the instant specification , it is well know in the art at the time the invention was made that peripheral lymphoid organ cells include T and B lymphocytes, NK cells dendritic cells , macrophages and stromal cells (see page 14, lines 15-20 in particular). Thus, it is the examiner position that one

skill in the art would immediately recognized that WO'589 teaches a three-dimensional cell culture system that is suitable for culturing peripheral lymphoid organ cells.

As has been stated in the previous Office Action, WO'589 teaches a method of culturing **peripheral lymphoid organ cells** on a three-dimensional scaffolding which is covered with culture medium (see entire document, Abstract and page 3 in particular). WO'589 teaches a culture medium comprising growth factors and cytokines, for example IL-2 or IL-4 (see pages 4 and 17 in particular). WO'589 teaches a method of producing antigen-specific T cells, comprising culturing T cells with antigen, wherein said antigen is presented by APC (see pages 5 – 6, and 22 in particular). WO'589 teaches that said antigen is a tumor antigen (see page 22 in particular). WO'589 teaches that three-dimensional structure formed from different porous particles and material including ceramic (see pages 15 and 16 in particular).

Claims 19 and 20 are included because the claimed functional limitation would be inherent properties of the referenced method of culturing cells. It is noted that the referenced and claimed method using the same culturing conditions. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

The reference teaching anticipates the claimed invention.

9. Claims 1-7 and 13-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/15629 or US Patent 5,160,490 (IDS) for the same reasons set forth in the previous Office Action, mailed on 08/01/06.

Applicant's arguments, filed 02/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that: the Examiner appears to rest the rejection on the assumption that the bone marrow – derived hematopoietic stem cells taught by WO'629 and US Patent '490 are peripheral lymphoid organ cells. Said assumption is incorrect as is evidence from the Declaration of DR. Bottaro under 37 C.F.R 1.132.

The examiner strongly disagrees with Applicant's interpretation of the Examiner's rejection . Moreover, the Examiner failed to find any support for said assumption in the previous Office Action rejection mailed on 08/01/06. It is the Examiner position that WO' 629 and US Patent '490 do not limited the disclosed method for culturing only hematopoietic stem cells. WO' 629 explicitly teaches that the disclosed three-dimensional culture system is suitable for

culturing **differentiated cells** of hematopoietic organ, T cells plasma cells erythrocytes, polymorphonuclear leukocytes, monocytes , macrophages etc. (see pages 6, 8, 15 and 29 in particular). Similarly, US Patent '490 teaches that the disclosed three-dimensional culture system is suitable for culturing differentiated cells, such as endothelial cells, macrophages, monocytes, T cells, stromal cells etc (see columns 9, 12, 18, 24 and 34 in particular) As is evidenced form the instant specification , it was well know in the art at the time the invention was made that peripheral lymphoid organ cells include T and B lymphocytes, NK cells dendritic cells , macrophages and stromal cells (see page 14, lines 15-20 in particular). Thus, it is the examiner position that one skill in the art would immediately recognized that WO'629 and US Patent '490 each teaches a three-dimensional cell culture system that is suitable for culturing peripheral lymphoid organ cells.

As has been stated in the previous Office Action , WO' 629 teaches a method of culturing cells, including T lymphocytes on a three-dimensional scaffolding which is covered with culture medium (see entire document, Abstract and page 4, 15 and 28 in particular). WO'629 teaches that three-dimensional structure formed from different porous particles and material including ceramic (see pages 7 and 9 in particular). WO' 629 teaches a culture medium comprising growth factors and cytokines (see page 12 in particular). WO' 629 teaches that culturing cells in three-dimensional matrix allows cells to have cell-cell contact in the three dimensions and is beneficial for growth and maintenance of cell culture (see page 4 in particular).

US Patent '490 teaches a method of culturing cells, including T lymphocytes on a three-dimensional scaffolding which is covered with culture medium (see entire document, Abstract and columns 5 and 9 in particular). US Patent '490 teaches that three-dimensional structure formed from different porous particles and material including ceramic (see columns 9 and 10 in particular). US Patent '490 teaches a culture medium comprising growth factors and cytokines (see column 13-14, 16 in particular). WO' 629 teaches that culturing cells in three-dimensional matrix allows cells to have cell-cell contact in the three dimensions and is beneficial for growth and maintenance of cell culture (see column 9 and 10 in particular).

Claims 19 and 20 are included because the claimed functional limitation would be inherent properties of the referenced method of culturing cells. It is noted that the referenced and claimed method using the same culturing conditions. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

The references teaching anticipates the claimed invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 6, 8-12 and 24-30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/15629 or US Patent 5,160,490 (IDS) in view of US Patent 6,821,778 for the same reasons set forth in the previous Office Action, mailed on 08/01/06.

Applicant's arguments, filed 02/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that since WO 99/15629 and US Patent 5,160,490 are not prior art references they can not be used for 103 rejection.

Contrary to Applicant's assertion, as has been discussed supra, it is the Examiner position that WO 99/15629 and US Patent 5,160,490 are prior art references and thus can be used in 103 rejection.

The claimed invention differs from the reference teaching in that WO 99/15629 or US Patent 5,160,490 does not explicitly teaches a method of culturing lymphoid organ cells on a three-dimensional matrix in the medium containing an antigens that are presented by antigen presenting cells.

US Patent' 778 teaches a method of producing an antigen-specific lymphocytes, comprising culturing T cells in the medium with antigens that are presented by antigen presenting cells (see entire document, Abstract in particular). US Patent' 778 teaches that various type of antigens including tumor antigens that can be presented by APC (see column 10 in particular). US Patent '778 teaches that obtained antigen-specific lymphocytes can be used for various uses, including immunotherapy (see column 5 in particular).

US Patent '378 teaches a method of producing an antigen-specific lymphocytes, comprising culturing T cells in the medium with antigens that are presented by antigen presenting cells (see entire document, Abstract in particular). US Patent'378 teaches that various type of antigens including tumor antigens that can be presented by APC (see column 14 –15 in particular). US Patent '778 teaches that obtained antigen-specific lymphocytes can be used for various uses, including immunotherapy (see column 7 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '778 and US Patent '378 to those of WO 99/15629 or US Patent 5,160,490 to obtain a claimed method of producing an antigen-specific lymphocytes, comprising culturing lymphoid organ cells on a three-dimensional matrix in the medium containing an antigens that are presented by antigen presenting cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because culturing lymphocytes in the medium containing antigens , wherein said antigens are presented by APC would generate an antigen-specific lymphocytes that can be used for various treatment, including immunotherapy as taught by US Patent '778 and US Patent '378. Culturing said lymphocytes and APC can be done on a three-dimensional matrix which is covered with culture medium, as taught by WO 99/15629 or US Patent 5,160,490 . The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor; Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

4/10/07